REMARKS/ARGUMENTS

Claims 1, 9-10, 20, 22, 25, and 27-28 have been amended.

Objections

Objected claims 5, 23, and 26 have been cancelled and objected non-elected sequences such as SEQ ID NOs: 5, 6, 7, 8, 9, 11 and 12 have been deleted from the claims on file.

Reconsideration and withdrawal of this objection is therefore respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner has rejected former claims 1, 5-11 and 22-31 as failing to comply with the written description requirement. This rejection has been considered and the claims have been further amended to restrict the oligonucleotide inhibitor to an antisense oligonucleotide and/or a siRNA molecule, said oligonucleotide inhibitor comprising the sequence set forth in SEQ ID NO: 10 described in the specification.

Reconsideration and withdrawal of this rejection is therefore respectfully requested.

The Examiner has rejected former claims 22-31 as failing to enable one skilled in the art to use the invention commensurate in scope with these claims. This rejection has been considered and reconsideration is respectfully requested on the following grounds.

First, Claim 25 has been amended and the term "preventing" has been deleted.

Second, the specification shows that treatment of human non-small cell lung carcinoma A549 cells with the antisense derived from SEQ ID NO:10 (referred to as A6 in the specification, see Table 1 or page 42) results in the inhibition of MBD2/demethylase mRNA expression (see Example 1, pp 42-43 of the specification and Fig. 4) *in vivo*.

Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph and § 101

The Examiner has rejected former claims 11, because the claim was indefinite for lack of an active, positive step. This rejection has been considered and the claim has been cancelled.

Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Rejections under 35 U.S.C. § 102

The Examiner has rejected former claims 1-2 and 5 under 35 U.S.C. § 102(b) as being anticipated by Zannis et al.. This rejection has been considered and the claims have been amended to be restricted to SEQ ID NO:10. Zannis et al. does not teach SEQ ID NO:10 and only teaches or suggests a different sequence.

Reconsideration and withdrawal of this rejection is therefore respectfully requested.

The Examiner has rejected former claims 1-2 and 5 under 35 U.S.C. § 102(e) as being anticipated by Wohlgemuth et al.. This rejection has been considered and the claims have been amended to be restricted to SEQ ID NO:10. Wohlgemuth et al. does not teach SEQ ID NO:10 and only teaches or suggests a different sequence.

Reconsideration and withdrawal of this rejection is therefore respectfully requested.

The Examiner has rejected former claims 1-2, 8-11, 22, 24-25, 27-29 and 31 under 35 U.S.C. § 102(e) as being anticipated by Bigey et al.. This rejection has been considered and the claims have been amended to be restricted to SEQ ID NO:10. Bigey et al. does not teach SEQ ID NO:10 and only teaches or suggest a different sequence. An alignment between the reverse complement of SEQ ID NO:10 and the region of interest of SEQ ID NO:1 of Bigey et al. is shown here:

```
reverse complement of SEQ ID NO:10:    aggggagggggagagtg
                                       ||| ||||||||||||||
Bigey SEQ ID NO:1:                     aggaggaggggagagtg
```

Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Rejections under 35 U.S.C. § 103

The Examiner has rejected former claims 1-11, and 22-31 under 35 U.S.C. § 103(a) as being unpatentable over Slack et al. in view of McKay et al., Walton et al. and Elbashir et al.. This rejection has been considered and reconsideration is respectfully requested on the following grounds:

First, the claims have been amended to be restricted to SEQ ID NO:10.

Second, the Examiner alleges that McKay et al. teaches that most preferred target region of a gene for antisense oligonucleotides includes the 5'-UTR. McKay et al. teaches that, generally, there are five regions of a gene that may be the target for antisense modulation: the 5'-UTR, the translation initiation region (tIR), the open reading frame (ORF), the translation termination codon (tTR) and the 3'-UTR (see column 5, lines 12-17). Essentially, this represents the entire mRNA minus the poly(A) tail. McKay et al. does not teach that the 5'-UTR represents a superior site for selection of potential antisense oligonucleotide selection, merely that it represents a site of selection amongst four other.

Moreover, SEQ ID NO:10 is not located in the 5'-UTR of the MBD2/demethylase messenger RNA. The 5'-UTR finishes at the translation initiation start site (AUG), which is located about 40 bases further upstream from SEQ ID NO: 10. Consequently, the claimed invention could not possible be obvious from the teachings of McKay et al..

Third, as the Examiner indicated in the present Office Action by including a quote from Opalinska et al.: the ability of nucleic acid molecules to modify gene expression *in vivo* is quite variable and therefore wanting in terms of reliability. Furthermore, the unpredictability of the *in vivo* inhibitory activity of this class of molecule remains unresolved, according to the very recent teachings of Schmidt (2007) cited by the Examiner. These views are further supported by data presented in the instant application. Two antisense molecules, SEQ ID NOs: 9-10 are targeted to a nearby region of the mRNA (see Fig. 3, A5 and A6 respectively), and the modification to gene expression of SEQ ID NO:10 is 3.2 time more important than that of SEQ ID NO:9 (Fig.

4). Significantly variable outcomes such as these ones could result in one inhibitor working as a therapeutic, while the other would not.

Most novel idea may appear simple and obvious after they have been proposed and reduced to practice. However, in the instant example used by the Examiner where the 5'-UTR of the MBD2/demethylase mRNA is targeted, one of ordinary skill in the art could have needed to test several dozens, if not hundreds of potential oligonucleotides before finding an appropriate inhibitor. The high variability of this technology that is acknowledged in the recent art is an indication that when the invention was reduced to practice, it would not have been obvious for one of ordinary skill in the art, to identify through routine screening and optimization the oligonucleotide inhibitor of SEQ ID NO:10, even in the limited target region delimited by the 5'-UTR. This task would have been further accentuated had the other four regions of the mRNA targeted as well, as was done in the case of the present invention.

Thus, it is submitted that the Slack et al. in view of McKay et al. in view of Walton et al. in view of Elbashir et al. would not render the claimed subject matter obvious to one of ordinatry skill in the art.

In view of the foregoing, the application is respectfully submitted to be in condition for allowance, and prompt, favorable action thereon is earnestly solicited.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

If there are any questions regarding this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned at (514) 871-2929 so that such questions can be expeditiously resolved.

FEE AUTHORIZATION

Should any fees associated with the submission be required, the Commissioner is authorized to charge such deficiencies to our Deposit Account No. 02-2095. Any overpayments should be credited to said Deposit Account.

Respectfully submitted,

Moshe Szyf et al.

By 
France Côté
Reg. No. 37,037
Tel: 514-871-2929